Journal of Current Veterinary Research

ISSN: 2636-4026

Journal home page: http://www.jcvr.journals.ekb.eg

Surgery

Local Administration of Curcumin for Treatment of Acute Superficial Flexor Tendon Injuries in Donkey: An Experimental Study.

Mohammed A. Noby, Amany S. Mawas, Elhussein E. Mahmoud*.

Department of Surgery, Anesthesiology and Radiology, Faculty of Veterinary Medicine, South Valley University, 83523 Qena, Egypt.

*****Corresponding Author:* e.badry@vet.svu.edu.eg *Received: 10/12/2024 Accepted: 11/2/2025*

ABSTRACT:

Superficial digital flexor tendon (SDFT) injuries are the most common injury of equine tendons because of exposure to repetitive trauma. Therefore, the study was aimed to investigate the effect of local application of curcumin (CUR) on donkey tendon injuries. Six adult donkeys were used in this study. Circular defects were created in SDFT at the level of midmetacarpus using biopsy punch (3mm). Immediately, after performing the defect, curcumin paste was applied locally inside the defect. An ultrasonographic examinations were recorded at 60 and 120 days postoperatively, then histopathological evaluation was performed using HE and Masson's trichrome stains. With transverse ultrasound images, complete filling of the SDFT defect with new informed tissue was noticed after application of CUR through absence of the hypoechoic zone at 120th day. However, the anechoic and hypoechoic zones were detected at the site of the defect at 60 days. Local application of curcumin improved healing of the tendon injury.

Keywords: Tendon injury; Lameness; Curcumin; Ultrasonography; Donkey model.

INTRODUCTION:

Tendon injuries are one of the most common problems in equine field especially flexor tendons leading to hinder athletic performance and early retirement of the animals. Equine surgeons continue to face difficulties with the slow healing process of injured tendons, particularly with traditional treatments that result in the creation of scar tissue that is less elastic, less biochemically and mechanically superior to normal tendon tissue, and more likely to re-injure (Rees et al., 2006). Recently, new biological treatments started to be used for tendon injuries such as curcumin which can improve the quality of tendon rupture healing, and thus represents a new technique in the dealing with injured tendon tissue (Jiang et al., 2016). Histological and biomechanical results showed that, oral administration of curcumin had better results for achilles tendon healing in the rat model (Güleç et al., 2018). Also, several studies were used curcumin as a therapeutic treatment option for wound healing (Ghallab et al., 2024), fatty liver (He et al., 2024), cancer (Liu et al., 2023), digestive disorders (Lopresti et al., 2021), pulmonary diseases (Lelli et al., 2017), Periodontitis (Boșca et al., 2019), neurodegenerative disease

(Azzini et al., 2024; Tizabi et al., 2014), and diabetes mellitus (Marton et al., 2021), depending upon unique properties as anti-inflammatory and anti-oxidant activities.

There is a limited data concerning the use of CUR for tendon defects in case of large animal model. therefore, the aim of work was to evaluate the ultrasonographic and histopathological findings of experimentally induced superficial digital flexor tendon defects at the level of mid-metacarpus in a working donkey model after local administration of curcumin with follow-up to 120th day.

MATERIALS & METHODS:

This controlled laboratory investigation was conducted with ethical consent from the Faculty of Medicine, Assiut University, in accordance with institutional guidelines for the care and use of experimental animals (04-2025-300597).

Creation of superficial flexor tendon defect in donkeys:

Six adult donkeys were used in this study. Firstly, the posture and gait of animals were examined from all views. Make sure that all the selected donkeys for this study were free from all external lesions especially those concerning the musculoskeletal system. These animals were subjected to experimental induction of SDFT defects at the mid-metacarpus using general anesthesia (Xylazine + Ketamine combination). The animals were positioned in a lateral recumbency. Experimental operations were performed in one forelimb in all animals through creation of circular defect about 3 mm in diameter by using of biopsy punch in superficial digital flexor tendon at midmetacarpus of apparent healthy donkeys, then SDFT defect was treated using 100 mg curcumin as a paste. Then the paratenon and subcutaneous tissue were closed separately using absorbable suture material (3-0 polyglactin 910 Egysorb; Taisier-Med) continuously. The skin was closed in a simple interrupted pattern using braided silk no. 0 (Ethicon/India) with applying of the bandage to avoid contamination.

Ultrasonographic assessment:

It was used for examination of SDFT of the affected limb at 60th and 120th day after the operation by using of Mindray (Portable Diagnostic System, 50-60Hz frequency) at department of surgery, Faculty of Veterinary Medicine, South Valley University.

Histopathological evaluation of the repaired tendon:

After 120 days, all donkeys were euthanized and part of the SFDT were collected, fixed in neutral buffered formalin 10%, then dehydrated in graded alcohols, embedded in paraffin blocks, and finally stained with HE and Masson's trichrome stains to evaluate quality of the repaired tendon.

RESULTS:

Ultrasonographic findings:

After topical application of curcumin, presence of anechoic and hypoechoic zone at the site of the defect were detected at 60th day. While absence of hypoechoic zone was noticed with improved echogenicity at the site of defects at 120th day, indicating reparative tissue formation (Figure 1).

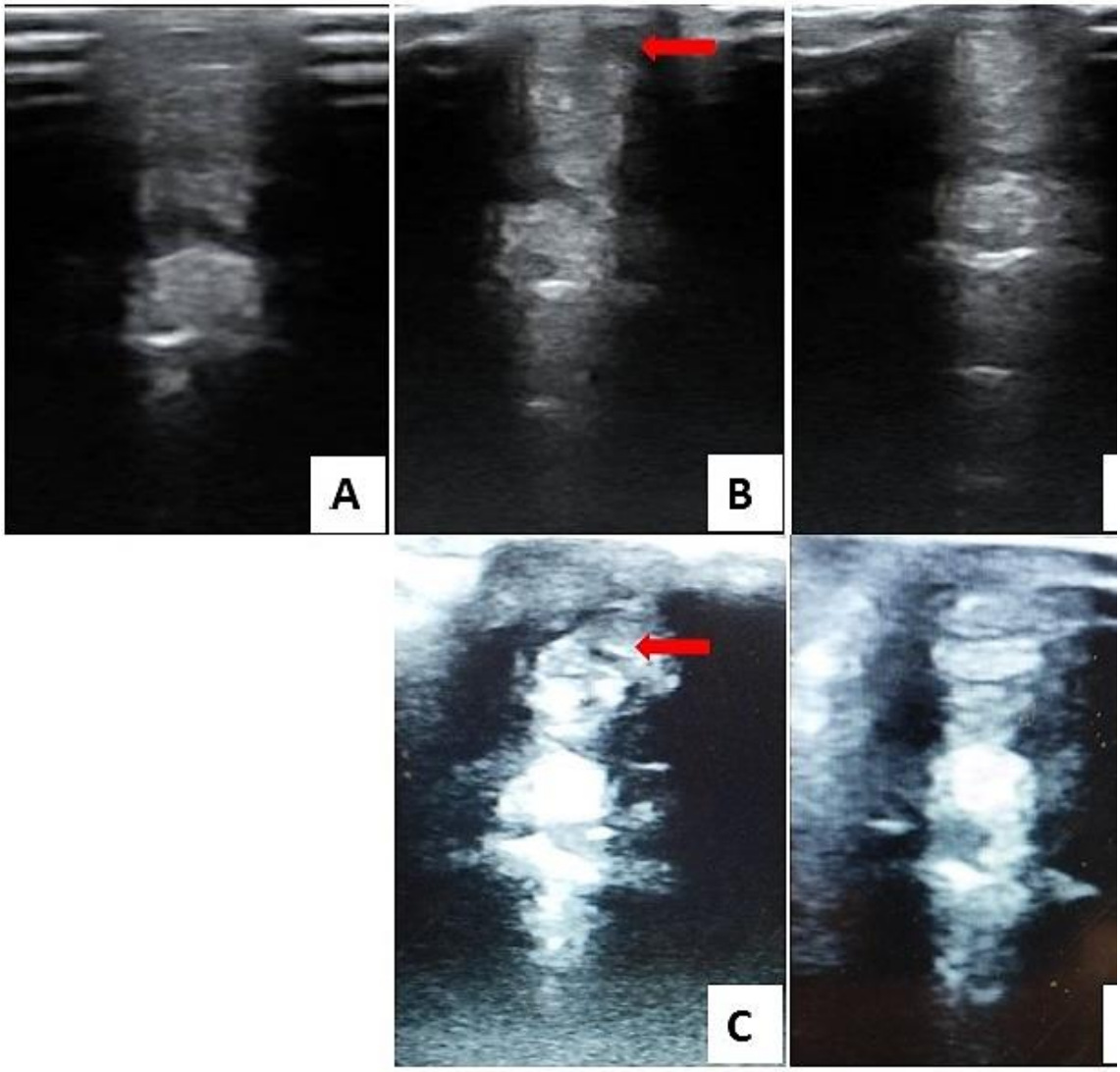

Figure 1: Normal sonography of SDFT in donkey model with echogenic appearance and composed of a uniform distribution of pinpoint white echoes (A). After curcumin application, SDFT showed presence of anechoic and hypoechoic zone at the site of the defect at 60 days (Arrow indicates SDFT defect) (B & C). While at 120 days CUR showed absence of the hypoechoic zone and an improve in echogenicity at site of the defect (D & E).

Histopathological evaluation of the repaired tendon:

With curcumin treatment, an obvious good healing areas with mild regular collagen bundles and mild inflammatory reaction around the defect in comparison to normal group in which collagen bundles were more regular ones using HE and Masson's trichrome stains (Figure 2).

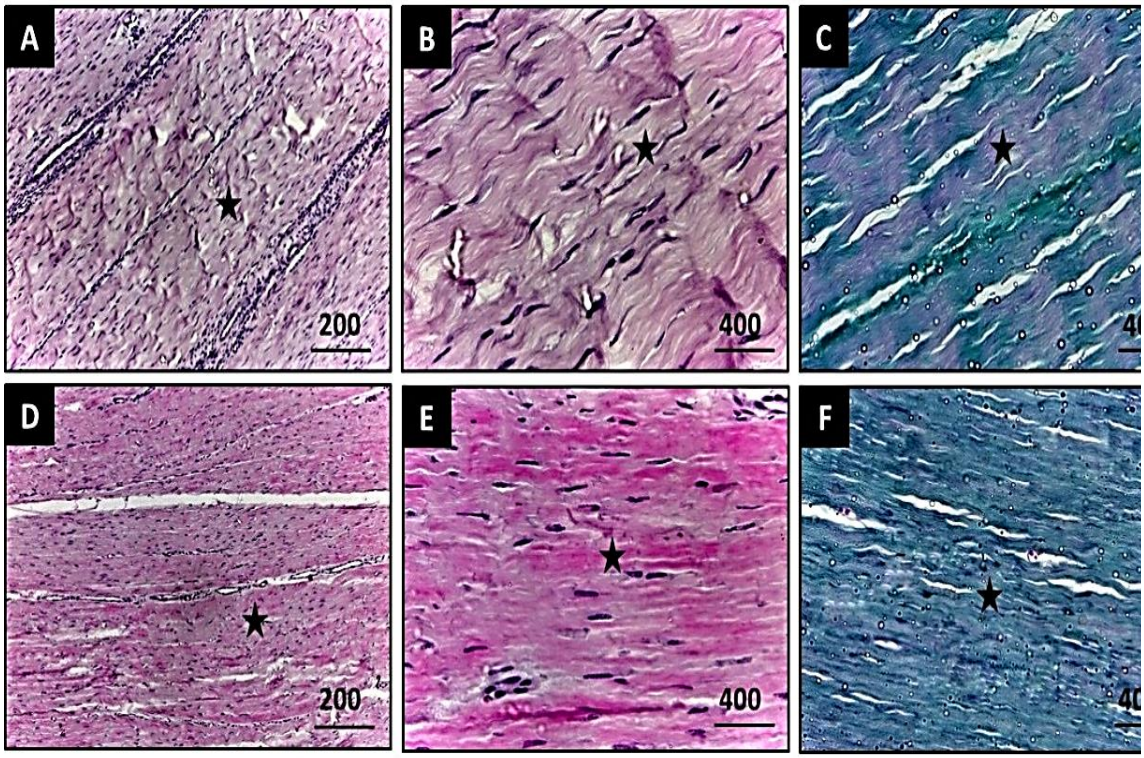

Figure 2: Histopathological lesions of SDFT in donkeys at the 120th day illustrated good healing areas with mild regular collagen bundles with local application of curcumin inside the tendon defect in comparison to normal one in which collagen bundles were more regular ones (star). A, B & C: Curcumin; D, E & F: normal group; A, B, D & E: H&E stain; C & F: Masson's trichrome stain.

DISCUSSION:

The present study demonstrated the treatment of circular surgically created defect in the SDFT at the level of midmetacarpus in the working donkeys using local application of curcumin depending upon ultrasonographic and histopathological assessments, led to complete filling of the defect with newly formed tissue at 120 days postoperatively. These results indicated that, there was a hypoechoic zone at the sites of defects in all groups 60 days postoperatively. While the hypoechoic zone reduced and disappeared completely by the day 120 postoperatively indicating the beneficial acceleration of the healing process in the induced defects with nearly normal echogenicity.

Moreover, concerning the role of natural products such as curcumin in the tendon healing were mentioned in the previous reports which indicated that, curcumin can boost collagen production, promote angiogenesis, reduce reactive oxygen species, and improve the healing of the neighboring tissues (Scharstuhl et al., 2009; Ma et al., 2013).

Ultrasonography is a valuable diagnostic tool in the clinic, and its evaluation gives us quantitative information about newly formed tendon and the extent of tendon lesions, but it doesn't give us information about the quality of the new tissue. So, to evaluate the quality of new tissue with respect to cell density, neovascularization, fiber organization, inflammatory aggregation, and

collagen type, further investigations will be based on histological evaluation (de Mattos et al., 2016). In the present study, good healing was observed after curcumin treatment of SDFT injuries with mild regular bundles with somewhat good density but not reach to the normal one confirmed by using HE and Masson's trichrome stain. In addition to, mild inflammatory reaction was observed around defect site that may be due to traumatic in origin. On the other hand, curcumin has been shown to enhance the expression of anti-inflammatory cytokines like interleukin (IL)-4 and decrease the expression of proinflammatory cytokines including tumor necrosis factor (TNF-α), IL-17A, IL-1β, and IFN-γ (Gao et al., 2015; Sun et al., 2013). Also, Curcumin may prevent IL-1β-induced human tenocyte inflammation and apoptosis (Buhrmann et al., 2011).

Extensive further studies will be performed on applying curcumin with mesenchymal stem cells to reach out superior result for tendon injuries resembling the native one with high density and regular collagen bundles. Also, long-term evaluation around 12 months must be put in the consideration due to long intricate healing process of the tendon with immunohistochemical assessment of the collagen type.

CONCLUSION:

Depending upon ultrasonography and histopathology, curcumin accelerates healing of SDFT injuries in working donkeys.

REFERENCES:

Azzini, E.; Peña-Corona, S.I.; Hernández-Parra, H.; Chandran, D.; Saleena, L.A.K.; Sawikr, Y.; Peluso, I.; Dhumal, S.; Kumar, M.; Leyva-Gómez, G.; Martorell, M.; Sharifi-Rad, J. and Calina, D. (2024). Neuroprotective and anti-inflammatory effects of curcumin in Alzheimer's disease: Targeting neuroinflammation strategies. *Phytother. Res.,* 38(6): 3169-3189.

Boșca, A.B.; Ilea, A.; Soriță̆u, O.; Tatomir, C.; Miklášová, N.; Pârvu, A.E.; Mihu, C.M.; Melincovici, C.S. and Fischer-Fodor, E. (2019). Modulatory effect of curcumin analogs on the activation of metalloproteinases in human periodontal stem cells. *Eur. J. Oral Sci.,* 127(4): 304-312.

Buhrmann, C.; Mobasheri, A.; Busch, F.; Aldinger, C.; Stahlmann, R.; Montaseri, A. and Shakibaei, M. (2011). Curcumin modulates nuclear factor kappaB (NF-kappaB)-mediated inflammation in human tenocytes in vitro: role of the phosphatidylinositol 3-kinase/Akt pathway. *J. Biol. Chem.,* 286(32): 28556-28566.

Carvalho, A.de M.; Hussni, C.A. and Alves, A.L.G. (2016). Adipose tissue as mesenchymal stem cells source in equine tendinitis treatment. *Semina: Ciências Agrárias*, 37(6): 4179-4192.

Gao, S.; Zhou, J.; Liu, N.; Wang, L.; Gao, Q.; Wu, Y.; Zhao, Q.; Liu, P.; Wang, S.; Liu, Y.; Guo, N.; Shen, Y.; Wu, Y. and Yuan, Z. (2015). Curcumin induces M2 macrophage polarization by secretion IL-4 and/or IL-13. *J. Mol. Cell Cardiol.,* 85: 131-139.

Ghallab, M.R.; Abdel-Hady, A.A.; Youssef, M.; Salah, M. and Mawas, A.S. (2024). Clinical and histopathological assessment of the combined therapeutic effect of Curcumin Nanoparticles and PRP on the cutaneous wound repair in rats. *Journal of Advanced Veterinary Research,* 14(4): 591-596.

Güleç, A.; Türk, Y.; Aydin, B.K.; Erkoçak, Ö.F.; Safalı, S., and Ugurluoglu, C. (2018). Effect of curcumin on tendon healing: an

experimental study in a rat model of Achilles tendon injury. *International orthopaedics,* 42(8): 1905-1910.

He, Y.; Chen, X.; Li, Y.; Liang, Y.; Hong, T.; Yang, J.; Cao, Z.; Mai, H.; Yao, J.; Zhang, T.; Wu, K.; Zou, J. and Feng, D. (2024). Curcumin supplementation alleviates hepatic fat content associated with modulation of gut microbiota-dependent bile acid metabolism in patients with nonalcoholic simple fatty liver disease: a randomized controlled trial. *Am. J. Clin. Nutr.*, 120(1): 66-79.

Jiang, D.; Gao, P.; Lin, H. and Geng, H. (2016). Curcumin improves tendon healing in rats: a histological, biochemical, and functional evaluation. *Connective tissue research,* 57(1): 20-27.

Lelli, D.; Sahebkar, A.; Johnston, T.P. and Pedone, C. (2017). Curcumin use in pulmonary diseases: State of the art and future perspectives. *Pharmacol. Res.*, 115: 133-148.

Liu, C.; Rokavec, M.; Huang, Z. and Hermeking, H. (2023). Curcumin activates a ROS/KEAP1/NRF2/miR-34a/b/c cascade to suppress colorectal cancer metastasis. *Cell Death Differ.*, 30(7): 1771-1785.

Lopresti, A.L.; Smith, S.J.; Rea, A. and Michel. S. (2021). Efficacy of a curcumin extract (Curcugen™) on gastrointestinal symptoms and intestinal microbiota in adults with self-reported digestive complaints: a randomised, double-blind, placebo-controlled study. *BMC Complement Med Ther.*, 21(1):40.

Ma, J.; Liu, J.; Yu, H.; Wang, Q.; Chen, Y. and Xiang, L. (2013). Curcumin promotes nerve regeneration and functional recovery in rat model of nerve crush injury. *Neuroscience letters,* 547, 26-31.

Marton, L.T.; Pescinini-E-Salzedas, L.M.; Camargo, M.E.C.; Barbalho, S.M.; Haber, J.F.D.S.; Sinatora, R.V.; Detregiachi, C.R.P.; Girio, R.J.S.; Buchaim, D.V. and Cincotto Dos Santos Bueno, P. (2021). The Effects of Curcumin on Diabetes Mellitus: A Systematic Review. *Front. Endocrinol. (Lausanne),* 12: 669448.

Rees, J.D.; Wilson, A.M. and Wolman, R.L. (2006). Current concepts in the management of tendon disorders. *Rheumatology,* 45(5): 508-521.

Scharstuhl, A.; Mutsaers, H.A.; Pennings, S.W.; Szarek, W.A.; Russel, F.G. and Wagener, F.A. (2009). Curcumin-induced fibroblast apoptosis and in vitro wound contraction are regulated by antioxidants and heme oxygenase: implications for scar formation. *Journal of cellular and molecular medicine,* 13(4): 712-725.

Sun, J.; Zhao, Y. and Hu, J. (2013). Curcumin inhibits imiquimod-induced psoriasis-like inflammation by inhibiting IL-1beta and IL-6 production in mice. *PLoS One,* 8(6): e67078.

Tizabi, Y.; Hurley, L.L.; Qualls, Z. and Akinfiresoye, L. (2014). Relevance of the anti-inflammatory properties of curcumin in neurodegenerative diseases and depression. *Molecules,* 19(12): 20864-20879.